



21 August, 2007

Securities and Exchange Commission Division of Corporate Finance Office of International Corporate Finance 450 Fifth Street, N.W. Washington D.C. 20549 U.S.A.



EXPRESS POST

Dear Sir/Madam,

Re: Metabolic Pharmaceuticals Limited (FILE NO. 82-34880)

submission of information filed with Australian Stock Exchange (ASX) and Australian Securities and Investment Commission (ASIC) pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934



Please find attached copies of announcements lodged with the ASX and ASIC:

Date of Announcement/Lodgement	To:	Title ·	No of Pages
10 September 2007	ASX	Appendix 3Z – Final Director's Interest Notice	3
10 September 2007	ASX	Appendix 3Z – Final Director's Interest Notice	!3
20September 2007	ASX	Update on Oral Peptide Delivery Platform	5

Yours faithfully,

Metabolic Pharmaceuticals Limited

**Belinda Shave** 

Financial Controller & Company Secretary

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(MPSEC21-9-07.doc)



Facsimile	
To	Company Secretary
Company	METABOLIC PHARMACEUTICALS LIMITED
Fax number	0398605777
From	ASX Limited - Company Announcements Office
Date	10-Sep-2007
Time	09:18:34
Subject	Confirmation Of Receipt And Release Of Announcement
Number of pages	1 only

ASX Limited ABN 98 008 624 691 20 Bridge Street Sydney NSW 2000

PO Box H224 Australia Square NSW 1215

Telephone 61 2 9227 0334 www.asx.com.au

DX 10427 Stock Exchange Sydney

#### **MESSAGE:**

We confirm the receipt and release to the market of an announcement regarding:

Final Director's Interest Notice RE

If ASX considers an announcement to be sensitive, trading will be halted for 10 minutes.

If your announcement is classified by ASX as sensitive, your company's securities will be placed into "pre-open" status on ASX's trading system. This means that trading in your company's securities is temporarily stopped, to allow the market time to assess the contents of your announcement. "Pre-open" is approximately 10 minutes for most announcements but can be 50 minutes (approximately) for takeover announcements.

Once "pre-open" period is completed, full trading of the company's securities recommences.

In accordance with Guidance Note 14 of ASX Listing Rules, it is mandatory to elodge announcements using ASX Online. Fax is available for emergency purposes and costs A\$38.50 (ncl. GST). The only fax number to use is 1900 999 279.

## Appendix 3Z

### Final Director's Interest Notice

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 30/9/2001.

Name of entity	METABOLIC PHARMACEUTICALS LIMITED	·—
ABN	96 083 866 862	

We (the entity) give ASX the following information under listing rule 3.19A.3 and as agent for the director for the purposes of section 205G of the Corporations Act.

ARTHUR EMMETT	
8 November 2005	
28 August 2007	
	8 November 2005

Part 1 - Director's relevant interests in securities of which the director is the registered holder In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Note: In the case of a company, interests which come within paragraph (i) of the definition of "notifiable interest of a director" should be disclosed in this part.

Number & class of securities
357,692 Fully Paid Ordinary Shares (ASX Code: MBP)

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

### Part 2 - Director's relevant interests in securities of which the director is not the registered holder

Note: In the case of a company, interests which come within paragraph (ii) of the definition of "notifiable interest of a director" should be disclosed in this part.

In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Name of holder & nature of interest Note: Provide details of the circumstances giving rise to the relevant interest	Number & class of securities
Name of Holder: The West Wialong A/C	136,500 Fully Paid Ordinary Shares (ASX Code: MBP)
Nature of Interest: Indirect Holding	

### Part 3 - Director's interests in contracts

Detail of contract	NIL
Nature of interest	
Name of registered holder (if issued securities)	
No. and class of securities to which interest relates	

Appendix 3Z Page 2

<sup>+</sup> See chapter 19 for defined terms.



Facsimile	
То	Company Secretary
Company	METABOLIC PHARMACEUTICALS LIMITED
Fax number	0398605777
From	ASX Limited - Company Announcements Office
Date	10-Sep-2007
Time	09:18:43
Subject	Confirmation Of Receipt And Release Of Announcement
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#### **MESSAGE:**

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Final Director's Interest Notice

CB

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## Appendix 3Z

### **Final Director's Interest Notice**

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Introduced 30/9/2001.

Name of entity	METABOLIC PHARMACEUTICALS LIMITED	
ABN	96 083 866 862	,

We (the entity) give ASX the following information under listing rule 3.19A.3 and as agent for the director for the purposes of section 205G of the Corporations Act.

CHRISTOPHER BELYEA
17 November 2006
30 August 2007

Part 1 – Director's relevant interests in securities of which the director is the registered holder In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Note: In the case of a company, interests which come within paragraph (i) of the definition of "notifiable interest of a director" should be disclosed in this part.

Number & class of securities

224,077 Fully Paid Ordinary Shares (ASX Code: MBP)

103,691 unquoted Performance Rights (ASX Code: MBPAA)

190,104 Unquoted Performance Rights (ASX Code: MBPAB)

<sup>+</sup> See chapter 19 for defined terms.

### Part 2 - Director's relevant interests in securities of which the director is not the registered holder

Note: In the case of a company, interests which come within paragraph (ii) of the definition of "notifiable interest of a director" should be disclosed in this part.

In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Name of holder & nature of interest Note: Provide details of the circumstances giving rise to the relevant interest	Number & class of securities
Name of Holder: Tate & Belyea Superannuation Fund	240,000 Fully Paid Ordinary Shares (ASX Code: MBP)
Nature of Interest: Superannuation Fund	

### Part 3 - Director's interests in contracts

Detail of contract	NIL
Nature of interest	
Name of registered holder (if issued securities)	
No. and class of securities to which interest relates	

Appendix 3Z Page 2 11/3/2002

<sup>+</sup> See chapter 19 for defined terms.



Facsimile	UND WARM SETTING LICE EVELVIATE
To	Company Secretary
Company	METABOLIC PHARMACEUTICALS LIMITED
Fax number	0398605777
From	ASX Limited - Company Announcements Office
Date	20-Sep-2007
Time	10:36:26
Subject	Confirmation Of Receipt And Release Of Announcement
Number of pages	1 only

ASX Limited
ABN 98 008 624 691
20 Bridge Street
Sydney NSW 2000

PO Box H224 Australia Square NSW 1215

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Update on Oral Peptide Delivery Platform

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ASX Announcement ASX code: MBP

# **Update on Oral Peptide Delivery Platform**

- Results from rodent studies showing that several peptide drugs modified by Metabolic have oral availability from 10 percent to greater than 30 percent, clinically and commercially significant levels
- Next steps include testing in larger animal species, and exploring additional peptide drugs for modification
- Detailed animal data available in a presentation at <u>www.metabolic.com.au</u>

Melbourne, 20 September 2007. Metabolic Pharmaceuticals Limited ("Metabolic") today announced new animal data regarding its proprietary Oral Peptide Delivery Platform.

Metabolic is developing a technology that may be used to create oral versions of injectable peptide drugs. Most peptide drugs are only effective when injected and are not absorbed well when swallowed. Metabolic has used the *Oral Peptide Delivery Platform* to create oral versions of several peptide drugs, including insulin and *ACV1* (formerly developed for neuropathic pain). The modified oral versions of these drugs have been tested in various rodent studies and demonstrated promising levels of oral availability, from 10 percent to greater than 30 percent, which is a clinically and commercially significant level. Data from these rodent studies are explained further in this announcement.

Mr Rob Stewart, Chairman of Metabolic, commented "the Company has been increasing its research around the *Oral Peptide Delivery Platform* since establishing proof-of-concept, in rodents, in late 2006. During this time, we have obtained encouraging data and the Board believes this platform holds sufficient potential value to warrant further investment. This project is now our primary objective, and accordingly the majority of Metabolic's research activities will be dedicated to the further development of the platform in the medium-term".

Dr Roland Scollay, CEO of Metabolic, said "if we can successfully generate oral versions of even a small proportion of the peptide drugs available, this platform could foster a number out-licensing opportunities. This is an early stage programme, and we don't expect any modified peptide drugs to reach clinical development for some time. However, we will continue to report our progress in preclinical studies and there may well be partnering opportunities for these compounds at the preclinical stage".

### What are peptide drugs and how does the Oral Peptide Delivery Platform work?

A peptide is a molecule made up of two or more amino acids. Large peptides, with more than 40 or 50 amino acids, are usually called proteins. The distinction is that peptides are short strings of amino acids and proteins are long strings. A significant part of food eaten is protein, for example lean meat, and the human digestive system is good at breaking protein down for absorption. This is one of the reasons peptide drugs are usually not effective when swallowed, as they are broken apart by digestive enzymes or acid in the stomach and intestines before they have a chance to be absorbed.

There are 600-700 injectable peptide drugs on the market or in development, including very commercially valuable drugs such as insulin. These drugs would be more convenient and potentially more profitable if they were effective when swallowed. In 2005, the total global market for protein and peptide drugs was estimated to be US\$57 billion. The combined sales of various insulin drugs amounted to US\$7.3 billion, with

industry analysts forecasting an increase to US\$13.6 billion by 2010. The vast majority of these drugs, including insulin, need to be injected.

Metabolic's *Oral Peptide Delivery Platform* is based on an understanding of the structure of Metabolic's drug, *AOD9604*, a peptide drug currently being developed to prevent and/or treat osteoporosis, and previously investigated for obesity. This peptide drug was found by Metabolic to be inherently orally available, which means *AOD9604* is effective even when swallowed. Around four years ago, Metabolic began exploring the hypothesis that the oral availability of *AOD9604* resulted from the presence of a particular lipophilic (fat soluble) stretch of amino acids. This understanding led to the modification of other peptide drugs such as insulin, by attaching this lipophilic amino acid sequence. Rodent studies with various modified peptide drugs have demonstrated promising levels of oral availability (the percentage of drug which gets to the target site in the body in active form after being swallowed) ranging from 10 percent to greater than 30 percent, which is a clinically and commercially significant level.

### Promising data from rodent studies testing Metabolic's modified peptide drugs

Clear proof-of-concept for the *Oral Peptide Delivery Platform* was established in late 2006 using a modified oral version of *ACV1*, a peptide drug that Metabolic had been developing for neuropathic pain. Whilst the clinical programme for *ACV1* has been subsequently closed, the drug is effective in rat models of neuropathic pain and this remains a good model for illustrating the application of the platform. In its original form, *ACV1* had to be administered by subcutaneous injection as it was only two percent orally available. Metabolic used the *Oral Peptide Delivery Platform* to create a version of *ACV1* which, in rodent studies, demonstrated oral availability in excess of 30 percent, based on dose responses in pharmacodynamic, or efficacy, readouts.

Following the success with the modified version of ACV1, Metabolic tested this approach on a number of other peptide drugs, with encouraging success. An oral version of insulin, a much larger, 51 amino acid protein, was created and tested in mice. In these mouse studies the oral availability of Metabolic's modified versions of insulin range between 10-20 percent with a very high level of consistency between animals. Indications from the scientific literature and analyst commentary suggest that reliable oral availability levels of 10 percent or more would be commercially viablefor insulin. Oral availability of unmodified insulin is no more than about 1 percent. The Company is currently undertaking further studies with its modified versions of insulin to achieve a more accurate measure of the oral availability under different conditions and to see if further improvements can be made or are needed.

Detailed data from the above mentioned rodent studies are available on <a href="www.metabolic.com.au">www.metabolic.com.au</a> or by contacting Metabolic directly on +61 3 9860 5700.

### Competitive advantages

The Company believes that there are three potential key competitive advantages of Metabolic's *Oral Peptide. Delivery Platform* compared to other technologies in development to modify peptide drugs. These are:

### 1. Higher levels of oral availability than other technologies

Results reported by other companies developing similar technologies have generally not demonstrated oral availability at the levels obtained using Metabolic's Oral Peptide Delivery, Platform.

### 2. Delivery approach

Metabolic's delivery approach is specific to the particular drug. Many other approaches to the oral delivery of peptide drugs involve generic changes to the gastric environment or absorption, giving rise to concerns about the facilitation of transport of other, unwanted peptides from the gastrointestinal tract. Metabolic's approach works without the addition of such generic absorption enhancing agents.

### 3. Safety

A wide variety of other approaches have been used by scientists and companies in attempts to make peptides orally available. Many of these have safety concerns, especially with anticipated long-term use. A potential advantage of the *Oral Peptide Delivery Platform* is that *AOD9604*, the drug on which the technology is based, has been tested in almost 1,000 humans, for periods up to six months, with no safety or tolerability issues reported. This testing was completed in a number of Phase 1 and Phase 2 human clinical trials for *AOD9604*, which is the peptide drug that forms the basis of this platform. *AOD9604* contains the lipophilic, oral sub-fragment used in this technology and was administered orally to all the obese subjects. Although it is not conclusive that there will not be safety or tolerability issues in the future with the sub-fragment added to other peptides, it is an encouraging indication.

### **Next steps**

The Metabolic Board has reviewed this technology, with extensive help from outside experts, including a detailed technical and data assessment by Professor Ashley Dunn, a life-science and biotechnology consultant who has had a long career in laboratory based, biomedical science, most recently as Associate Director of the *Ludwig Institute for Cancer Research* and Head of its Molecular Biology Program. Professor Dunn said "the data I have reviewed in detail is of good quality and the technology looks very promising, even though still at a relatively early stage. The Company's approach to validating the platform is sound."

On the basis of that analysis and other reviews commissioned by the Board, the Company has committed A\$2 million over the next 12 months to determine whether this technology can be taken to the next stage. There are a number of milestones that should be reached during that time which will guide the Board as to the appropriate levels of investment going forward.

The immediate next steps for development of the Oral Peptide Delivery Platform are:

### Further studies to measure blood levels of the modified drugs

The data described above are based on measuring the actual effects of the drug in various, quite robust, physiological responses, rather than measuring drug levels in the blood. Apparently as a result of the special properties of the sub-fragment being added to the peptide drugs, Metabolic's modified peptide drugs appear to be difficult to detect in blood. Experiments are in progress to develop better ways to measure the drugs in the body.

### Studies in larger animals

Most of the data for the *Oral Peptide Delivery Platform* has been obtained from experiments in rats or mice. Further studies are currently being planned to extend the proof-of-concept in larger animals. If successful, such studies would suggest that modification using the platform may be effective for humans. However, it is impossible to confirm its applicability in the human context until these modified peptide drugs are actually tested in humans.

In addition, the Company will investigate modified versions of additional peptide drugs, and will seek to learn more about the mechanisms underlying the transport of these oral versions into the body. Significant further progress in the above-mentioned studies is expected over the next 6-12 months. The *Oral Peptide Delivery Platform* is a research project at the preclinical stage and no drug candidates are expected to be ready for clinical trials for at least two years. However, clear proof-of-concept with some of these drugs could lead to licensing or partnering opportunities much sooner. This project is currently the key priority for Metabolic and accordingly the majority of Metabolic's research activities will be dedicated to developing this platform in the medium-term. Progress with the platform will be reported as further milestones are achieved.

### Risk profile

This project remains at the preclinical level and has a high element of risk. Translation of the results to a higher species of animals and then humans remains to be shown. On the other hand, once established as a platform in humans, it may have a lower risk profile if oral versions of known drugs are developed as the efficacy and safety profiles are known and the main risk is being able to deliver the drugs with this technology. Therefore, with existing peptides, risk may be significantly reduced once Phase 1 studies have been successfully completed whereas with novel drugs, high levels of risk remain throughout the clinical trial process. Despite the risk levels, the Metabolic Board has resolved to take this project to the next stage, as the potential for value if the project is successful is very large whilst the short-term investment is relatively low.

### More information available

A detailed presentation has been prepared with data on each rodent study, and is available at <a href="https://www.metabolic.com.au">www.metabolic.com.au</a> or by contacting the Company directly on +61 3 9860 5700.

### For further information, contact:

Diana Attana, Assistant Company Secretary/IRO diana.attana@metabolic.com.au
T: +61 3 9860 5700

#### **About Metabolic**

Metabolic Pharmaceuticals Limited (ASX: MBP, NASDAQ OTC: MBLPY) is a Melbourne based, ASX listed biotechnology company with 300 million shares on issue. Metabolic's focus is to take drug candidates through research, formal preclinical and clinical development.

### Inherent Risks of Investment in Biotechnology Companies

There are many inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Metabolic are dependent on the success of their research projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in companies specialising in these, such as Metabolic, must be regarded as highly speculative. Metabolic strongly recommends that professional investment advice be sought prior to such investments.

#### Forward-looking statement

Certain statements in this ASX Announcement may contain forward-looking statements regarding the Company's business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing the Company's goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Metabolic undertakes no obligation to publicly update any forward looking statement, whether as a result of new information, future events, or otherwise. Actual results could differ materially from those discussed in this update. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the Metabolic Pharmaceuticals Limited Annual Report for the year ended June 30, 2006, copies of which are available from the Company or at <a href="https://www.metabolic.com.au">www.metabolic.com.au</a>.

